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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/805,801	03/13/2001	Mary Collins	GNN-016	2860

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EXAMINER
GAMBEL, PHILLIP

ART UNIT	PAPER NUMBER
1644	11

DATE MAILED: 06/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/805801	Applicant(s) COLLINS
	Examiner GAMBEL	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If the period for reply specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 4/14/03

2a)☑ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) _____ is/are pending in the application. 1-5

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 1-5

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

Paper No. 11

DETAILED ACTION

1. Applicant's amendment, filed 4/10/03 (Paper No. 10), has been entered.
Claims 1-5 have been amended.

Claims 1-5 are pending and being acted upon as they read on the election species

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 4/10/03 (Paper No. 10).
The rejections of record can be found in the previous Office Action (Paper No. 8).

3. Claims 1-5 are rejected under 35 U.S.C. § 102(e) as being anticipated by Sayegh et al. (U.S. Patent No. 6,280,957 (see entire document).

Applicant's arguments, filed 4/10/03 (Paper No. 10), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant notes that Sayegh et al. teach administration of antibodies that binds B7-1 and B7-2 with rapamycin in combination with intravenous injection of donor hematopoietic stem cells and optionally, an inhibitor of CD40:CD40L interaction. However, applicant argues that Sayegh et al. Neither teach nor suggest administration of antibodies that B7-1 and B7-2 in the absence of donor hematopoietic stem cells.

As pointed out previously, it is noted that the claimed methods recite "comprising" which leaves the claim open for the inclusion of unspecified ingredients even in major amounts. See MPEP 2111.03.

Sayegh et al. teach methods of transplanting grafts, including intestines (see columns 3-4, overlapping paragraph), with blockers of the CD28-B7 interactions, including anti-B7-1 and/or anti-B7-2 antibodies (see column 1, lines 55-61; column 3, lines 45-48) and immunosuppessive agents capable of inactivating T cells, including rapamycin (see column 4, paragraph 2). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods to transplant intestines with combination therapies, including the use of anti-B7-1 and anti-B7-2 antibodies and rapamycin.

Given the breadth of the instant claims, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure.

In contrast to applicant's assertions; disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. See In re Susi USPQ 423 (CCPA 1971). A known or obvious composition does not patentable simply because it has been described as somewhat inferior to some other product for the same use. See In re Gurley 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). See MPEP 2123.

Applicant's arguments are not found persuasive.

4. Claims 1-5 are rejected under 35 U.S.C. § 103(a) as being unpatentable over de Boer et al. (U.S. Patent No. 5,869,050; 1449) in view of Lenschow et al. (Transplantation 60: 1171-1178, 1995; 1449) Tarumi et al. (Transplantation 67: 520-525, 1999) AND/OR Newell et al. (J. Immunol. 163: 2358-2362, 1999).

Applicant's arguments, filed 4/10/03 (Paper No. 10), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant argues that both the suggestion and the reasonable expectation of success must be founded in the prior art and not in applicant's disclosure, which is not satisfied by the prior art of record.

Applicant agues that the ordinary artisan would not have been motivated to specifically target signaling by B7-1 and B7-2 to prolong intestinal allograft transplants.

Citing Yin et al. (Transplantation 62: 1537-1539, 1996) (Appendix B); applicant asserts that the nature of the immune response to intestinal allografts seems to be unique compared to other types of allografts, whereby results obtained from experiments with other types of allografts cannot be extrapolated to transplantation of intestinal grafts.

Applicant argues that both Newell et al. And Tarumi et al. would not have motivated the ordinary artisan to try to prolong intestinal allograft acceptance using antibodies to B7-1 and B7-2, given the limitations of CTLA4Ig on intestinal allograft survival in these references in experimental models

Applicant argues that there would not have been an expectation of success at the time the invention was made, given the distinction between biological processes between intestinal allografts and other allograft tissues / organs, since in the cited prior art CTLA-4, which was known to block both B7-1 and B7-2 induced costimulation, was insufficient to prevent intestinal allograft rejection.

Applicant also argues that Tarumi et al. Is inconsistent with the disclosures of Newell et al., Yin et al. and Sayegh et al.

Applicant asserts that present invention is based on a specific analysis of the involvement of B7-1 and B7-2 in intestinal allograft transplant rejection in a highly relevant mouse model system.

As pointed out previously, it is noted that the claimed methods recite "comprising" which leaves the claim open for the inclusion of unspecified ingredients even in major amounts. See MPEP 2111.03.

The prior art teach combination therapy, including the use of immunosuppressives such as rapamycin the transplantation of allografts, as taught by De Boer et al. which teach the use of B7-specific antibodies to inhibit transplant rejection, including combination therapy with known immunosuppressives such as rapamycin (see columns 6-7, Immunosuppressive Agents; Claims 6, 13) (see entire document, including Summary of the Invention, Detailed Description of the Invention and Claims).

Lenschow et al. teach the inhibition of transplant rejection with both B7-1-specific and B7-2-specific antibodies and that maximal inhibition of allogeneic responses was observed with the combination of both B7-1-specific and B7-2-specific antibodies (see entire document, including Abstract, Results and Discussion). It is noted that Lenschow et al. observed while anti-B7-1 antibody therapy had little effect of graft prolongation, a combination of anti-B7-1/anti-B7-2 antibodies significantly prolonged graft survival (see Abstract, Results and Discussion).

Also, Lenschow et al. notes that with in vivo therapy using a combination of anti-B7-1 plus anti-B7-2 monoclonal antibodies significantly prolonged the mean survival time of the grafts beyond either the CTLA-4Ig or anti-B7-2 alone (see page 1175, column 2, lines 33-36, last full sentence). Also, Lenschow et al. teach that it is clear that B7-1 plays a secondary but substantive role in allogeneic responses to islet cells in vivo (page 1176, column 1, lines 3-5).

Therefore, in contrast to applicant's assertions, the prior art provided sufficient motivation and expectation of success in combining anti-B7-1 and anti-B7-2 antibodies in inhibiting transplant rejection and that in vivo studies indicated that this combination of anti-B7 antibodies was significantly more effective than CTLA4Ig.

While there may have been limitations with CTLA4Ig in experimental murine models of intestinal allografts, Tarumi et al. and Newell et al. clearly provided sufficient motivation and expectation of success in targeting B7-1 and B7-2 in the transplantation of intestinal allografts.

Tarumi et al. teach the use of CTLA4Ig which inhibits the CD28:CTLA4-B7 pathway to induce the long-term acceptance of small bowel allografts (see entire document).

Newell et al. also teach the use of CTLA4Ig which blocks the CD28/B7 pathway, resulting in the prevention of intestinal allografts (see entire document).

Further Tarumi et all. teach that clinical bowel transplantation is accompanied by immunosuppression (e.g. see the first paragraph of the Discussion on page 522, column 2) and that a blockade of costimulatory signals were useful for suppression of alloreactive immune responses (e.g. see Discussion on page 522).

Again, the claims encompass combined immunosuppression, wherein the combined prior art provides clear motivation and expectation of success in therapeutic regimens of transplantation. In contrast to applicant's assertions, both Tarumi and Newell provide sufficient motivation and expectation of success that targeting both B7-1 and B7-2 would contribute to preventing or inhibiting intestinal graft survival.

Given that CTLA4Ig blocks both B7-1- and B7-2-mediated responses and given that the combination of anti-B7-1 and anti-B7-2 antibodies achieve significant inhibition of allogeneic responses and graft rejection; one of ordinary skill in the art would have been motivated to combine both B7-1-specific and B7-2-specific antibodies to inhibit transplant rejection, including intestinal transplant rejection. Given the teachings of de Boer et al, Lenschow et al., Tarumi et al. and Newell et al., the ordinary artisan would have an expectation of success in prolonging intestinal graft survival by blocking both B7-1- and B7-2-mediated interactions. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

5. No claim is allowed.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
June 23, 2003